

## **Varicella**

In the prevaccination era, an estimated 3 to 4 million cases of varicella occurred every year- basically the entire annual birth cohort. But vaccination coverage in 2003 was about 85%, and there is evidence from active surveillance sites that the disease is no longer inevitable.

Data from active varicella surveillance sites have shown a more than 85% decrease in the number of varicella cases. Incidence has declined in all age groups, but particularly among children 1 to 4 years of age. In addition, the number of outbreaks, the number of school days missed due to varicella, and the number and rates of hospitalization have fallen dramatically.

We do not think this reduction in varicella is unique to the active surveillance sites. Several states conducting passive surveillance for varicella have also seen a major decline in cases in the last 3 years. Despite this clear impact on varicella disease, providers and parents continue to have concerns about the vaccine. One of the most common concerns we hear about varicella vaccine has to do with waning immunity and breakthrough disease. We asked Dr. Dalya Guris, team leader for herpes virus activity for the National Immunization Program, to update us on recent investigations of these issues.

Varicella vaccine was approved for use in the United States in 1995. Prelicensure clinical trials estimated vaccine effectiveness at 80% to 90%. Therefore, 10% to 20% of vaccine recipients will develop varicella disease, also called breakthrough varicella. However, most breakthrough cases are mild with less than 50 lesions. Prelicensure trials estimated protection from moderate or severe varicella disease at up to 95%.

In the years since varicella vaccine was licensed, CDC and state and local health departments have investigated varicella outbreaks in a variety of settings, such as child care centers and schools. The purpose of these investigations was to estimate postlicensure vaccine effectiveness, and to try to identify risk factors for varicella vaccine failure.

Seventeen outbreak investigations have estimated vaccine effectiveness at 71% to 100% for all varicella disease, with most estimates around 85%. A large case control study among children in private medical practices in Connecticut also estimated overall effectiveness at 87%. Effectiveness against moderate or severe varicella has consistently been found to be 90% to 100%, verifying that breakthrough varicella is much less severe than varicella in unvaccinated people. Three outbreak investigations estimated vaccine effectiveness of 44% to 59%. The reason or reasons these three estimates are lower than all the others is not clear. However, we generally investigate outbreaks that are unusual, and these three outbreaks were not representative of typical varicella outbreaks.

Whenever possible during studies of varicella vaccine effectiveness, investigators have attempted to identify risk factors for vaccine failure. One of the potential risk factors for breakthrough varicella is time since vaccination. If breakthrough varicella increased with increasing time since vaccination, this would suggest waning of vaccine induced immunity over time. Four investigations have found that persons vaccinated 3 to 5 years earlier were more likely to develop

breakthrough varicella than those vaccinated more recently. However, the majority of investigations that were of sufficient size to investigate this issue did not identify time since vaccination as a risk for vaccine failure. The large case control study of Connecticut children found that effectiveness decreased from 97% in the first year to 84% in years two through 8 after vaccination.

Age of vaccination has also been a concern. Some children may still have circulating maternal antibody after the first birthday. If this is the case, children vaccinated closer to a year of age might have a higher risk of vaccine failure because of maternal antibody interference, than those vaccinated a few months later. Seven investigations have found a relation between age of vaccination and breakthrough varicella. Most have found the risk of breakthrough varicella 2 to 4 times higher among children vaccinated at 12 to 14 months of age compared to those vaccinated at age 15 months or older. However, this is also not a consistent finding in outbreak investigations. Most investigations have not identified age at vaccination as a risk factor for breakthrough varicella.

Another risk factor that has been suggested for varicella vaccine failure is the presence of asthma. Two investigations have found an increased risk of breakthrough varicella among children with asthma. However, these studies did not include information about medication, such as steroids, that the child may have been taking. A retrospective cohort study examined the effect of both asthma and systemic steroids. This study found an increased risk for children taking steroids but not for those with asthma who were not taking steroids.

Taken as a whole, these postlicensure investigations have confirmed prelicensure estimates of varicella vaccine effectiveness against all varicella disease, and especially against moderate and severe illness. Although the results of a few studies have suggested otherwise, most investigations have not identified age at vaccination or time since vaccination as risk factors for breakthrough varicella. It is not clear whether asthma or steroid use at the time of vaccination increases the risk of breakthrough disease. Until more definitive information become available, the Advisory Committee on Immunization Practices will continue to recommend a single dose of varicella vaccine for all children at 12 to 18 months of age. However, ACIP will continue to monitor research in this area to ascertain the possible benefit of changes in the recommended immunization schedule.